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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,400	07/22/2002	Thomas Hantke	0480/01219	2952

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EXAMINER	
WANG, SHENGJUN	
ART UNIT	PAPER NUMBER
1617	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/088,400	HANTKE ET AL.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6-8,10-16 and 20-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6-8,10-16 and 20-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' amendments and remarks submitted December 1, 2006 is acknowledged.

Specification Objections

1. The amendment filed September 1, 2006 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the change of time from min to hour in the table at page 15 lacks support from the application as originally filed. The examiner could not find any support from the specification for such change. The original data presented at page 15 is obviously not right, but the data presented in the amendment is not the obvious right answer, as other change also make sense, such as, change 1, 2, 3, 4, 5, 7, and 8 in the table to 100,200, 300, 400, 500, 600, 700, and 800.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections 35 U.S.C. 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1, 2, 4, 6-8, 10-16, 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Andries et al. (US 6,197,779), in view of Goertz et al. (US 4,801,460), Nakamichi et al. (US 5,456,923), Sasatani et al. (US 5,876,760) and Takada (US 5,350,741), and in further view of Baert (EP 0 872 233, IDS)

4. Andries et al. teaches the HIV inhibiting pyrimidine derivatives herein and the method of using the same for preparing pharmaceutical composition, and for treating HIV infection. See, the abstract, cols 1-10, 17-19. The elected compound herein is a preferred compound disclosed by Andries et al. see, col. 10, lines 14-15. The compounds may be formulated into various conventional dosage forms, such as powders, tablet, capsule with solid carrier and other pharmaceutical excipients. See, particularly, col. 18, line 19 to col. 19, line 25. (Applicants also admitted the compounds are known in the art, citing PCT/EP99/02043, which is equivalent to US 6,197,779, and PCT EP/02044, see page 2 herein)

5. Andries et al. do not teach expressly the particular dosage form herein with PVP or it's copolymer as carrier and polyoxyethylene hydrogenated castor oil and citric acid as additional excipients, or the particular release forms.

6. However, Goertz et al. teach a solid pharmaceutical form wherein polyvinylpyrrolidone or copolymer of vinylpyrrolidone and vinyl acetate or used as carrier, and a solid solution of the active ingredient is formed. See particularly, the abstract, col. 3, lines 3-31, col. 4, lines 11-45, and the claims. There is no particular limitation as to the active ingredients employed therein. The concentration of active ingredients may be in the rage from 0.1 to 95%, with preferred range of 30-70%. 45 to 50% of polymer is used in the particular examples. Other known pharmaceutical excipients may be added accordingly. The forms may be made by extrusion. See,

cols. 3-8. Nakamichi et al. teach that solid dispersion or solution is known to be useful for controlling the rate of release of a drug from dosage form or improving the bioavailability of drugs. Nakamichi et al. further teaches that other polymeric material, such as modified cellulose (e.g. hydroxypropylmethylcellulose) are similarly useful (like PVP) as solid carrier, and extrusion is a conventional method for making a solid dispersion or solution form. See, particularly, cols. 1-2, and the claims. Both Sasatani et al. and Takada teaches that polyethylene glycol castor oil ester and citric acid are known pharmaceutical excipients and are particularly known to be useful in solid form wherein Polyvinypyrrolidone is carrier. See, particularly, col. 5, lines 33-63 in Sasatani et al. and the claims in Takada.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to formulate a pharmaceutical dosage form of the compounds disclosed by Andries et al. into solid dispersion or solution in particulate form, wherein vinypyrrolidone polymer or copolymer is the carrier, and with additional other pharmaceutical excipients, such as polyoxyethylene hydrogenated castor oil, citric acid.
A person of ordinary skill in the art would have been motivated to formulate a pharmaceutical dosage form of the compounds disclosed by Andries et al. into solid dispersion or solution in particulate form, wherein vinypyrrolidone polymer or copolymer is the carrier, and with additional other pharmaceutical excipients, such as polyoxyethylene hydrogenated castor oil, citric acid, because polymeric carrier, such as vinylpyrrolidone polymer or copolymer, are known to produce solid dispersion or solution with a drug which provide controlled release and enhanced bioavailability. Further, the employment of various pharmaceutical excipients, such as polyoxyethylene hydrogenated castor oil (surfactants), and citric acid (acids), accordingly is

within the skill of artisan. The further employment of other polymers, such as hydroxypropylmethylcellulose, would have been obvious since the modified cellulose is known to be similarly useful as a solid carrier. Attention is directed to Baert, which teaches the employment of combination of PVP and hydroxypropyl methylcellulose as carrier for controlled release antiviral dosage form. See, particularly, the example (pages 6-7) and the claims. Furthermore, the optimization of a result effective parameter, e.g., drug releasing profile, or the effective amounts of the drug and the other ingredients therein, is considered within the skill of the artisan. See, In re Boesch and Slaney (CCPA) 204 USPQ 215.

The employment of a dosage form known to be useful for a particular purpose, in a pharmaceutical package useful for the same purpose is considered within the skill of the artisan. Further, the optimization of a dosage regimen for the administration of a dosage form is considered within the skill of the artisan, absent evidence to the contrary.

7. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Andries et al. (US 6,197,779), in view of Goertz et al. (US 4,801,460), Nakamichi et al. (US 5,456,923), Sasatani et al. (US 5,876,760) and Takada (US 5,350,741), and in further view of Baert (EP 0 872 233, IDS) for reason discussed above, and in further view of Jones et al.

Andries et al. Goertz et al. (US 4,801,460), Nakamichi et al. (US 5,456,923), Sasatani et al. (US 5,876,760), Takada (US 5,350,741), and Baert et al. do not teach expressly the particular K value of the polyvidone. It is noted that Kollidon VA64 is used in the solo example herein (page 14). It is reasonably believed that Kollidon VA64 meets the limitation of K value. Jones teaches polymers, such as Kollidon K30 and K90 and Kollidon VA 64, are particularly suitable as binder in antiviral composition for extrusion and formulation of particles. See, particularly,

col. 3, lines 56 to col. 4, line 2. Therefore it would have been obvious to use those well-known polyvidone for formulate a pharmaceutical dosage form of the compounds disclosed by Andries et al. into solid dispersion or solution in particulate form.

Response to the Arguments

8. Applicants' amendments and remarks submitted September 1, 2006 and December 1, 2006 have been fully considered, but are not persuasive.

9. Applicants argue that the rejections are improper because Baert et al. id directed to an composition comprising antiviral agent which is structurally different from the antiviral compounds herein, Applicants further contend that Crospolyvidone employed by Baert et al. is different from the polyvidone herein. The arguments are not probative.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). It is noted that Baert et al. was cited to show that the particular cellulose recited in claim 11 is a known pharmaceutical excipient. As stated above, considering the cited references as a whole, the claimed invention would have been obvious to one of ordinary skill in the art.

10. Applicants further argue the examiner's citation of, In re Boesch and Slaney (CCPA) 204 USPQ 215 is misused, as the parameters herein have not been clearly recognized. The examiner respectfully disagrees. The rejections state: "the optimization of a result effective parameter, e.g., *drug releasing profile, or the effective amounts of the drug* and the other ingredients therein, is considered within the skill of the artisan. See, In re Boesch and Slaney (CCPA) 204 USPQ 215."

Applicants have not provided probative arguments show that "*drug releasing profile, or the effective amounts of the drug*" is not result effective parameters.

11. Furthermore, applicants' amendment to the specification does not provide support for unexpected results as asserted previously by applicants.

First, the amendment introduces new matter; further, even if the amendment valid, the data does not support the asserted benefit. As noted there is no data for the first 7 hours for the sustained release form. It is not clear whether the dissolution rate was reached to 95% within first hour, second hour, or after the seventh hour.

Regarding the establishment of unexpected results, a few notable principles are well settled. It is applicant's burden to explain any proffered data and establish how any results therein should be taken to be ***unexpected and significant***. See MPEP 716.02 (b). The claims must be ***commensurate in the scope*** with any evidence of unexpected results. See MPEP 716.02 (d). Further, A DECLARATION UNDER 37 CFR 1.132 must compare the claimed subject matter with the closest prior art in order to be effective to rebut a prima facie case if obviousness. See, MPEP 716.02 (e).

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Shengjun Wang
Primary Examiner
Art Unit 1617